

DOCKET NO: 200427US0CONT



IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE APPLICATION OF :

CLAUDIO CAVAZZA

: EXAMINER: GOLLAMUDI KISHORE

SERIAL NO: 09/777,874 :

FILED: FEBRUARY 7, 2001

: GROUP ART UNIT: 1615

FOR: PHARMACEUTICAL  
COMPOSITION COMPRISING  
CARNITINE OR ALKANOYL L-  
CARNITINE, FOR THE PREVENTION  
AND TREATMENT OF DISEASES  
BROUGHT ABOUT BY LIPID  
METABOLISM DISORDERS

REPLY BRIEF

COMMISSIONER FOR PATENTS  
ALEXANDRIA, VIRGINIA 22313

SIR:

This Reply Brief responds to the Examiner's Answer mailed March 23, 2004.

Issues:

The Appellants acknowledge that the obviousness rejection of Claims 18 and 20-31 over Wiegand by itself, and Claims 28-29 over Wiegand in view of Moffett, have been withdrawn.

The Appellants believe that the obviousness rejection of claims 28-30 in view of Hastings, in view of Wiegand and Burtle, or in combination, has been withdrawn. However, confirmation of the withdrawal of this rejection and clarification of the written record is respectfully requested.

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Grounds of Rejection:

The following remarks pertain to each ground of rejection. The Appellants have previously demonstrated the superior and unexpected synergistic effects of the combination of acetyl-L-carnitine and hydroxycitric acid on the metabolism of lipids, see page 5, lines 6-12, of the specification; on reducing food consumption and on reducing body weight increase, see page 6, lines 5-9 and Tables 1 and 2 on pages 16 and 17 of the specification; and on achieving significant reductions in cholesterol and lipid (triglyceride) levels, see page 5, line 6-page 6, line 14 of the specification and Tables 3-5 on pages 18-20 of the specification. The synergistic effects provided by the invention are described on page 5, lines 13-16. As shown by the experimental data in the present disclosure, e.g., Tables, 2, 4 and 5, the combination of hydroxycitric acid and acetyl-L-carnitine produces a statistically significant synergistic effect that administration of hydroxycitric acid alone, or acetyl-L-carnitine alone, does not. However, these experimental data have not been accepted as being statistically significant by the Examiner.

As summarized on page 8 of the Appeal Brief, the combination of acetyl-L-carnitine and hydroxycitric acid provides superior reductions in body weight (Table 2), triglyceride levels (Table 4) and cholesterol levels (Table 5) compared to acetyl-L-carnitine or hydrocitric acid alone.

The statistical significance of the reported results was determined by the performance of the T-test, a conventional test of statistical significance of differences between groups.

The following Table from the Appeal Brief summarizes these results:

<u>Table 2: Body Weight Increase</u>	<u>Level</u>	<u>Reduction</u>	<u>%</u>
Control (no acetyl-L-carnitine or HCA)	62.8	-----	
Acetyl-L-carnitine only:	60.4	-2.4	3.8
HCA only:	46.6	-16.2	25.8
Combination of acetyl-L-carnitine and HCA:	31.6	-31.2	49.9

Table 4: Triglyceride level

Control (no acetyl-L-carnitine or HCA)	195.8	-----	
Acetyl-L-carnitine only:	191.2	-2.4	1.2
HCA only:	170.6	-25.2	12.9
Combination of acetyl-L-carnitine and HCA:	120.4	<b>-75.4</b>	38.5

Table 5: Cholesterol level

Control (no acetyl-L-carnitine or HCA)	270.5	-----	
Acetyl-L-carnitine only:	266.7	-3.8	1.4
HCA only:	196.6	-73.9	27.3
Combination of acetyl-L-carnitine and HCA:	150.5	<b>-120.0</b>	44.4

The Declaration filed January 2, 2002 establishes the statistical significance of the above summarized results by providing the T-test scores for each compared group. The statistical significance of these results as shown in the Declaration are "entitled to considerable probative value and are given considerably more weight than the opinion of the layman", In re Zeidler, 682 F.2d 961, 215 USPQ 490 (CCPA 1982); In re Neave, 370 F.2d 961, 152 USPQ 274 (CCPA 1967); In re Corkill, 771 F.2d 1496, 226 USPQ 1005 (Fed. Cir. 1985).

The Examiner's Answer indicated that based on a comparison of the reported "standard deviations" of the test results, that no statistically significant difference is seen. The Examiner's Answer indicated that the statistical method used by the Appellants (the T-test) is not being questioned, only the interpretation of the data. However, clearly the issue is whether the Appellants have shown statistically significant differences between the various control groups and the test group (acetyl-L-carnitine + hydroxycitric acid). Page 5, last three lines, of the Examiner's Answer indicates that the examiner is unable to determine the claimed statistical significance since it is unclear as to what the data are being compared to. For example, it is pointed out that Tables 2, 4 and 5 presented in the Declaration filed January 2, 2002 show that even controls have a  $p < 0.001$  and queries how is it possible to determine the statistical significance of results in view of a p value being reported for a control

The Appellants respond that since the test group (i.e., the group receiving the combination of acetyl-L-carnitine + hydroxycitric acid) is being compared to multiple control groups (i.e., groups receiving no acetyl carnitine or hydroxycitric acid; receiving acetyl-L-carnitine alone; or receiving hydroxycitric acid alone) that the simplest way to present the T-test data was to present the p values for each comparison along side the relevant control compared to the test group. For example, the p value of  $p < 0.001$  reported along side the first control ("Controls") in Table 2 of the prior-filed Declaration is that from the comparison of that control group (no acetyl-L-carnitine and no hydroxycitric acid) with the test group which received both acetyl-L-carnitine and hydroxycitric acid. This is explained on page 2, lines 1-2, of the Declaration filed January 2, 2002.

In view of the superior and unexpected effects of the synergistic combination of acetyl-L-carnitine and hydroxycitric acid as shown in the experimental data of record, and the statistical significance of these results as established by the T-test, the Appellants respectfully request the reversal of the obviousness rejections on appeal.

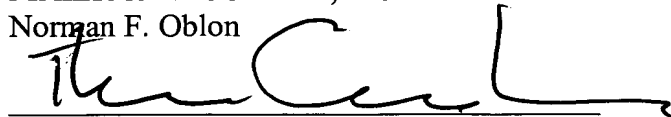
RELIEF REQUESTED

Reversal of the Examiner's rejections under 35 U.S.C. 103 of the appealed claims is respectfully requested.

Respectfully submitted,

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